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ARCHIVES OF PEDIATRICS

A MONTHLY DEVOTED TO THE

DISEASES OF INFANTS AND CHILDREN

JOHN FITCH LANDON, M.D., Editor

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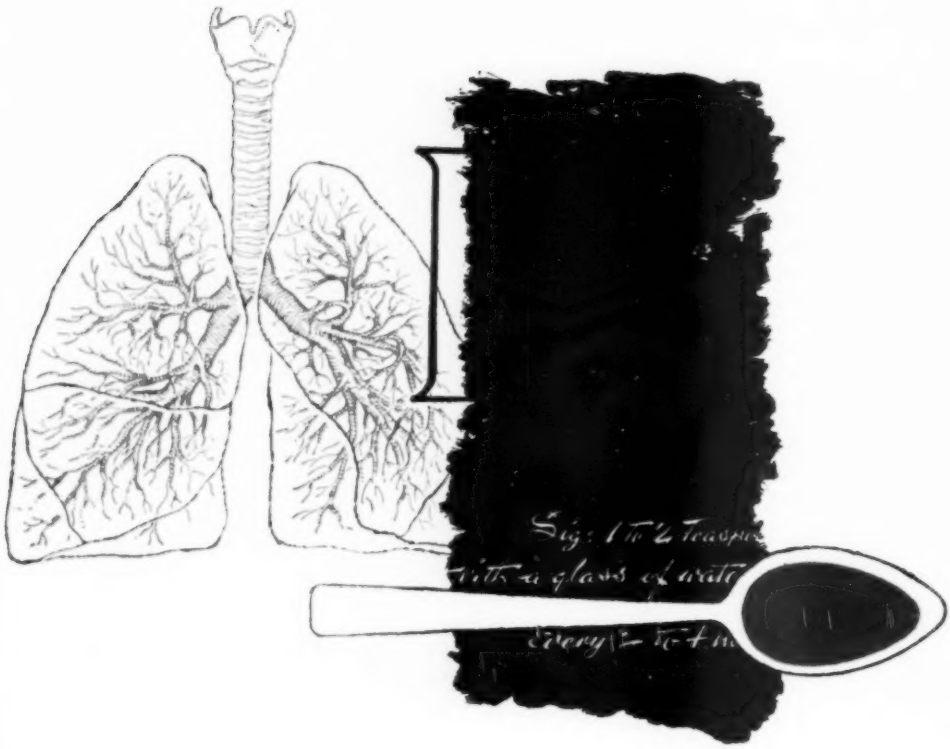

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in whooping cough

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VOL. 69 FEBRUARY 1952 No. 2

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COMPLICATIONS OF VARICELLA*

GANGRENE OR CELLULITIS OCCURRING SIMULTANEOUSLY IN THREE MEMBERS OF A FAMILY

JAMES B. GILLESPIE, M.D.

AND

G. L. PORTER, M.D.

Urbana, Ill.

Of the common contagious diseases in childhood chickenpox is generally regarded by parents and physicians as the one to be least feared. The illness is usually mild and requires only the most simple symptomatic treatment, and precautions to prevent its spread are frequently omitted. Nevertheless, in certain instances, complications are observed and an attitude of complete indifference to the potentialities of chickenpox is not justified.

In 1935 Bullowa and Wishik[1] reviewed the complications of varicella among 2,534 patients observed at the Willard Parker Hospital during a five-year period. In this series, 133 patients (5.2 per cent) suffered a complication. In order of frequency these were otitis media, abscesses, pneumonia, lymphadenitis, cellulitis, septicemia, erysipelas, encephalitis, appendicitis, gangrene, mastoiditis, impetigo, intestinal intoxication, paronychia, conjunctivitis, laryngitis, meningitis, empyema, nephritis, herpes zoster, osteomyelitis, balanitis, pericarditis, endocarditis, hordeolum, pharyngitis, blepharitis, stomatits and parotitis. Forty-one patients had more than one complication and the mortality in the entire series of patients with varicella was 0.4 per cent. Frequency of complications

*From the Department of Pediatrics and the Department of Ophthalmology, Carle Memorial Hospital and Carle Hospital Clinic, Urbana, Illinois.

at different age levels paralleled the incidence of the disease and, with few exceptions, the occurence of particular complications was not affected by the age of the patient. Pneumonia was noted in the younger children, particularly under 2 years of age, appendicitis occured in older children between 6 and 14 years of age, and herpes zoster occurred in adults. In all cases in which cultures were obtained, a hemolytic streptococcus was demonstrated; occasionally other organisms were also noted.

Surface complications, including skin, mucous membranes, subcutaneous tissue and lymph glands, comprised 57 per cent of all complications.[2] Cellulitis occurred in 19 per cent and gangrene in 5 per cent of those with surface complications.

Varicella with complications may occur in the newborn period. When a pregnant mother has chickenpox at the time of delivery the infant may develop chickenpox as early as eight days after birth.[3, 4] Death from purulent chickenpox with hemorrhages has been reported in a premature infant a few weeks of age.[5] A variety of intraocular eye conditions concomitant with or subsequent to chickenpox has been observed.

Complications from varicella probably occur more frequently than they are reported, although, judging from reports in the literature, surface complications are fortunately not common. The occurrence of surface complications in several members of a family simultaneously has not been noted in a review of the limited literature on the subject. Three members of the family here reported developed chickenpox and complications of gangrene or cellulitis simultaneously. These patients were seen in the pre-antibiotic era (1942) and consequently there were limitations to available therapy. The occurrence of complications in all the members of a family who developed chickenpox is sufficiently rare to justify calling attention to this possibility.

CASE REPORTS

Case No. 1. Mrs. P. L., age 33 years, a native of Chile who had been in the United States 6 months, was first examined in consultation on April 24, 1942. The husband was an officer in the Chilean Air Corps and stationed at Chanute Field, Illinois. There were two children in the family (Cases 2 and 3). The present illness dated

from April 11, 1942 and a diagnosis of chickenpox was made April 13. On April 14, cellulitis developed about a pock located on the right lower lid near the external canthus. Other skin lesions had resolved in the usual manner. The cellulitis became extensive, and on April 20 an incision was made in the right upper lid but pus was not obtained. The incision healed promptly. The vision of the right eye was reduced to light perception. On April 23, a physician examined the right fundus and observed "congestion of the retina." A paracentesis of the anterior chamber was performed on the same day with subsequent increase in the lid edema. On this date the patient first came under our observation.

Examination revealed marked edema and induration of the lid of the right eye. The edema was of such a degree that the lids could be separated only 2 mm. The cornea appeared clear and the anterior chamber of normal depth. A satisfactory view of the fundus was not obtained due to inadequate separation of the lids. Light perception was not present. The globe was markedly proptosed (estimated 10 mm.) and immobile. An area of localization in the outer third of the lower lid was apparent. Her general condition and appearance were not remarkable. Numerous areas of recently healed chickenpox were present. Examination of the nose and throat revealed no evidence of active sinusitis and temperature, blood count and urinalysis were within normal limits. A diagnosis of suppurative cellulitis of the eyelids with secondary involvement of the orbit was made. The possibility of cavernous sinus thrombosis was considered, but the absence of constitutional symptoms suggested that the disease was confined to the orbit.

Under intravenous pentothal anesthesia incisions were made in the central third of the lid and near the external canthus. Considerable pus was obtained from each incision. The abscess cavity extended nasally to the rim of the orbit and temporally one centimeter. Cautious probing revealed no extension through the septum orbitale and cultures which subsequently yielded a nonhemolytic streptococcus and a staphylococcus were obtained. Penrose drains were inserted through each incision. Sulfathiazole was administered in a dosage adequate to maintain a therapeutic blood level. Reduction of lid edema occurred subsequently for three days during which time profuse drainage continued. It was possible to

separate the lids sufficiently to view the fundus. The entire retina was edematous and the optic disc was pale. The macula had a "cherry red" appearance and the globe remained fixed.

On April 29 erythema nodosum, involving principally the lower extremities, developed. The abscess areas continued to drain without evidence of healing and an erythematous indurated area developed over the right temple. On May 5 this area was incised. A fistulous tract, extending from the lower lid temporally outside the lateral wall of the orbit, was observed. This extended posteriorly to the hair line where an incision was made. A second tract extended into the outer third of the upper lid and a second incision was made at the tip of the tract. Through and through drains were inserted between these areas (Fig. 1). Widespread necrosis of the subcutaneous tissues was present but frank pus was not encountered. On May 18 it was necessary to incise necrotic areas of the brow and near the inner canthus of the lower lid. Necrotic drainage persisted from these fistulous tracts until July 15, approximately 3 months after onset of the infection. On August 10 some proptosis persisted. Ocular rotations returned but were still impaired and a moderate ptosis was present. Vision was completely absent and the pupil dilated with a loss of all reflexes. There was marked pallor of the optic nerve and generalized narrowing of the retinal arteries suggestive of previous obstruction of the central artery.

The patient was last observed in November 1942, at which time further regression of the proptosis was noted and ptosis remained unchanged. Shortly afterward she returned to Chile.

Case 2. V. L., female, age 28 months, was first examined May 2, 1942 because of an "ulcerated" area on the abdomen subsequent to chickenpox. She was the second and youngest child of Case 1. The past medical and family histories were not contributory. This child, with her mother and an older sister, had developed chickenpox two weeks previously. Subsequent to scratching of the pruritic lesions on the lower abdomen, an ulcerated area developed just below the umbilicus and the lesion increased in size rather rapidly in the several days before examination.

Physical examination showed numerous scattered chickenpox crusts and a gangrenous area 3.5 x 5 cm. in the right midabdomen between the symphysis and the umbilicus. The lesion involved all

skin structures and extended to the muscle layers. A probe could be passed from 2.5 to 6 cm. laterally from the undermined periphery of the lesion. Drainage was slight and the wound appeared clean. Urinalysis showed specific gravity 1.026, acid reaction, trace albumin, negative sugar, 5-6 hyaline casts, 5-6 red blood

Fig. 1. Edema of lids and proptosis of globe. Appearance following incision and drainage.

cells and 40-50 pus cells. Hemogram showed hemoglobin 53 per cent (Sahli), erythrocytes 3,420,000, leukocytes 18,800, neutrophiles 77 per cent, lymphocytes 20 per cent and eosinophils 3 per

cent. Nonhemolytic staphylococci were obtained from cultures of the abdominal wound. Blood platelets were 380,000 per cu. mm. The bleeding time was 3 minutes and the coagulation time 2 minutes, 45 seconds.

She was hospitalized on the day of initial examination. Tem-

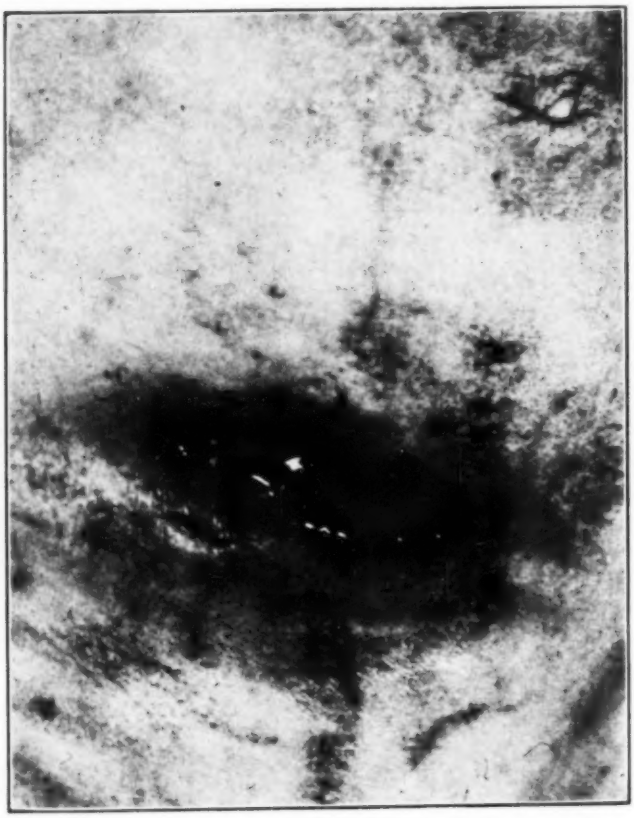

Fig. 2. Gangrenous area lower abdomen. Dark appearance at base of lesion due to gentian violet.

perature during the first two weeks of hospitalization varied between 37.7° and 38.5° C. General condition was fair, although there was anorexia and poor skin turgor. Infra-red light, a heat

cradle and zinc peroxide packs were used without apparent effect. By May 5 the lesion had extended laterally, dissecting skin and subcutaneous tissues from the fascial layers with marked peripheral induration. Therapy was changed to irrigations with a one per cent solution of sulfanilamide and repeated local applications of one per cent aqueous solution of gentian violet; she was transfused (Fig. 2).

Repeated blood transfusions were productive of rather striking improvement in her general condition, but little apparent change occurred in the gangrenous area. On May 18 swelling in the anterolateral areas of the abdomen were observed and purulent drainage from the wound had increased. After surgical consultation, bilateral incisions, approximately 8 cm. on either side of the necrotic area, were made in the abscesses at the sides of the abdomen. Considerable granulation tissue was curetted from the already undermined skin and Penrose drains were inserted from the lateral incisions through the osteum of the necrotic area. Copious amounts of sanguinopurulent drainage saturated the dressing. Irrigations with one per cent sulfathiazole and oral sulfathiazole were instituted. On May 22 the drains were removed, but the central wound had changed little in size or appearance. The wound was irrigated repeatedly with chlorinated soda (Dakin's solution) and by May 27 appeared much cleaner, drier, and free of necrotic debris. She was afebrile subsequent to May 27. On May 18, urinalysis was negative; blood count showed hemoglobin 80 per cent, erythrocytes 3,970,000, leukocytes 15,200 with neutrophiles 84 per cent, lymphocytes 15 per cent and monocytes 1 per cent. Dakin's solution irrigations and compresses were continued during the last two weeks of hospitalization.

On June 4, at dismissal from the hospital, the gangrenous area was much smaller and entirely dry. Dry dressings without local medication were utilized subsequent to dismissal. On June 9 a granuloma, 5.0 x 2.0 cm. was removed from the abdominal wound under ether anesthesia and sinuses extending from either extremity of the granulation to points at the anterior spine of the ileum bilaterally, were curetted. The wound continued to heal satisfactorily and healing was complete on June 18, 1942.

The patient was last observed October 19, 1942 at which time she was well and the wound entirely healed.

Case 3. R. L., age 6 years, the eldest daughter of Mrs. P. L. (Case 1) developed chickenpox about April 13, 1942. A week subsequent to the onset of the disease she developed an abscess with cellulitis of the right lower thigh just above the knee. The lesions required repeated incision and drainage and healing was prolonged. Cultures of the wound were not taken. All treatment was provide at the Station Hospital, Chanute Air Force Base, Rantoul, Illinois and information on this child was provided by a member of the medical staff of the hospital.

DISCUSSION

Among the extravascular causes of gangrene of the skin, the exotoxins of streptococcal and staphylococcal infections and the violent inflammations as variola, varicella and herpes zoster may be agents in production of such lesions.[6] Multiple gangrenous lesions occasionally complicate severe systemic diseases as typhus, typhoid fever, malaria and the acute exanthems. Dermatitis gangrenosa is an extremely rare complication of scarlet fever and it has been observed subsequent to meningococcemia.[7,8,9] Gangrenous ulcers may occur in the mouth of infants and children, especially as a complication of measles.[10] The term cancrum oris and noma have been applied to such lesions and occurrence is most frequent in debilitated infants. Varicella complicated by both acute thrombocytopenic purpura and gangrene has been reported.[11] A rapidly progessive streptococcic or staphylococcic cellulitis with central necrosis and gangrene may occur subsequent to surgical procedures or other trauma.[12]

Ocular complications are considered to be of very rare occurence in varicella.[13] Conjunctivitis and superficial punctate keratitis are minor complications. Vesicular lesions or phlyctenular-like pustules may involve the cornea or conjunctiva and their course is protracted. Severe visual loss may result from corneal involvement. Uveitis, with recovery, has been reported.[14] Ocular involvement may also occur when varicella is complicated by encephalomyelitis. Walsh[15] has observed cranial nerve palsies, nystagmus, optic neuritis and atrophy of varying degrees under these circumstances.

Berens[16] states that metastatic abscess of the orbit occurs occasionally but the condition is not discussed. Case reports of orbital cellulitis associated with varicella were not noted in the literature.

In the absence of encephalomyelitis the optic nerve involvement in Case 1 was undoubtedly secondary to orbital pathology. Unfortunately, we did not observe this patient until the disease was well established. At the time the fundus was first observed its appearance suggested previous occlusion of the central artery. This could have resulted from embolus, thrombophlebitis, or direct pressure. In event the latter was responsible, obstruction of the central vein should have been observed.

The occurence of severe complications from chickenpox in several members of a family simultaneously has not been noted in a review of the literature on that subject. Chickenpox is not regarded by physicians in Chile as a serious disease and complications are infrequent.[17,18]

The general nutrition of the reported patients appeared good and the economic status of the family and cleanliness in the home appeared above average. Unfortunately throat cultures were not taken from the mother, father or children but it is not unlikely that the streptococcus and staphylococcus were harbored in the nasopharynx of one or more members of the family.

Undoubtedly the handling of these patients would have been simpler and the end result more gratifying if antibiotics had been available in 1942. Marchionini[19] noted dramatic reduction in the mortality from noma associated with malaria and in dermatitis gangrenosa infantum when penicillin was used. All therapy used on the patients here reported seemed ineffective except incision, drainage, debridement and irrigation with chlorinated soda (Dakin's solution). This is essentially the treatment outlined by Meleny in his excellent discussion of hemolytic streptococcus gangrene.[20]

SUMMARY

Three members of a family, a mother and two children, who developed cellulitis or gangrene simultaneously subsequent to the onset of chickenpox, are reported. Literature on the subject of surface complications from varicella is briefly reviewed.

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CONGENITAL FIBROCYSTIC DISEASE OF PANCREAS. (Ugeskrift for Laeger, Copenhagen, 113: 1009, Aug. 2, 1951). Bastrup-Madsen and Mortensen state that congenital fibrocystic disease of the pancreas, a hereditary anomaly of development, occurs predominantly in infants, about equally often in the two sexes. Pulmonary symptoms are prominent. Diagnosis can often be made on the basis of the history and ordinary clinical examination. Examination of the duodenal secretion will reveal the inability of the pancreas to excrete enzymes, but collection of the secretion is often difficult or impossible in children. Examination of the proteolytic activity of the feces may be useful. Roentgen examination can support the diagnosis but is not decisive. The earliest recognizable manifestation of the disorder is meconium ileus in the newborn infant, which is treated operatively. The fully developed picture of the disorder, marked by failure to gain weight, foul, bulky, and fatty stools, constant cough, and recurring pulmonary infection, is usually seen in the first half year of life. The characteristic lesions are cystic fibrosis of the pancreas and bronchiectasis. Treatment is symptomatic. The pulmonary infection is as a rule the immediate cause of death, which occurs oftenest in the first year of life. The prognosis may not be so unfavorable as it seems today, as probably only the gravest and most typical cases are recognized. The disease is most readily confused with celiac disease, which, however, rarely occurs till toward the end of the first year of life and is not as a rule accompanied by pulmonary changes.—*Journal A.M.A.*

SCHOOL LUNCH PROGRAM IN THE SCHOOLS OF SAN FRANCISCO

J. C. Geiger, M.D.
AND
Kathleen Thody, B.S.
San Francisco.

The concept that one of the valuable functions of the school lunch program is to provide training in sound food habits has been advanced by many educators as well as members of the medical profession. They realize that eating with their friends helps children to learn to enjoy nutrition food. In San Francisco the establishment of centralized management under the coordinator of school lunch and home economics is in keeping with this philosophy. This cafeteria organization has many advantages:

(1) By having supervision of the lunchroom by home economics trained people, the highest food standards may be maintained.

(2) It brings about greater coordination of classroom activity (to give information about food needs) and cafeteria participation (to put this information into practice).

(3) Suggestions can be made to the people supervising the lunchroom to make the cafeteria most conducive to establishment of good eating habits.

In San Francisco, 43 schools—24 elementary and 19 secondary schools—operate cafeterias. All of these cafeterias are under the National School Lunch Program. The lunches under this program include and provide one-third to one-half of the daily food needs which include the following:

(a) One-half pint of whole milk as a beverage.

(b) Two ounces of lean meat, poultry, fish or cheese, or one egg, or one-half cup of dry beans or peas or four tablespoons of peanut butter.

(c) Three-fourths cup of vegetables or fruit or both.

(d) One or more portions of bread or muffins or other bread made of whole grain cereal or enriched flour.

(e) Two teaspoons of butter or fortified margarine.

Beyond these requirements, the starches can be added for filler.

These lunches are served at a minimum cost (25 cents in elementary schools, 30 cents in secondary schools) and free to

Director of Public Health, City and County of San Francisco (J. C. Geiger, M.D.). Nutritionist of the San Francisco Department of Health (Kathleen Thody, B.S.).

children who are unable to pay; a national subsidy and funds budgeted by the local school board make this program possible.

In the Spring of 1950, the Nutritionist from the San Francisco Department of Public Health visited some 15 cafeterias and found all were meeting the nutritional requirements of the program. Pupils in the schools participated by filling in daily food records. In addition to visiting the cafeterias the nutritionist reviewed 200 of these surveys in the elementary grades. Observations were made on the basis of the following three factors:

(1) How was a child's daily food intake influenced by taking the cafeteria plate lunch and by lunches from other sources—home-packed, store or lunch at home?

(2) What was the nutritional contribution of the lunches—plate lunches and lunches from other sources?

(3) To what extent does this program help children to learn foods needed for health and growth and assist them in making choices of such foods?

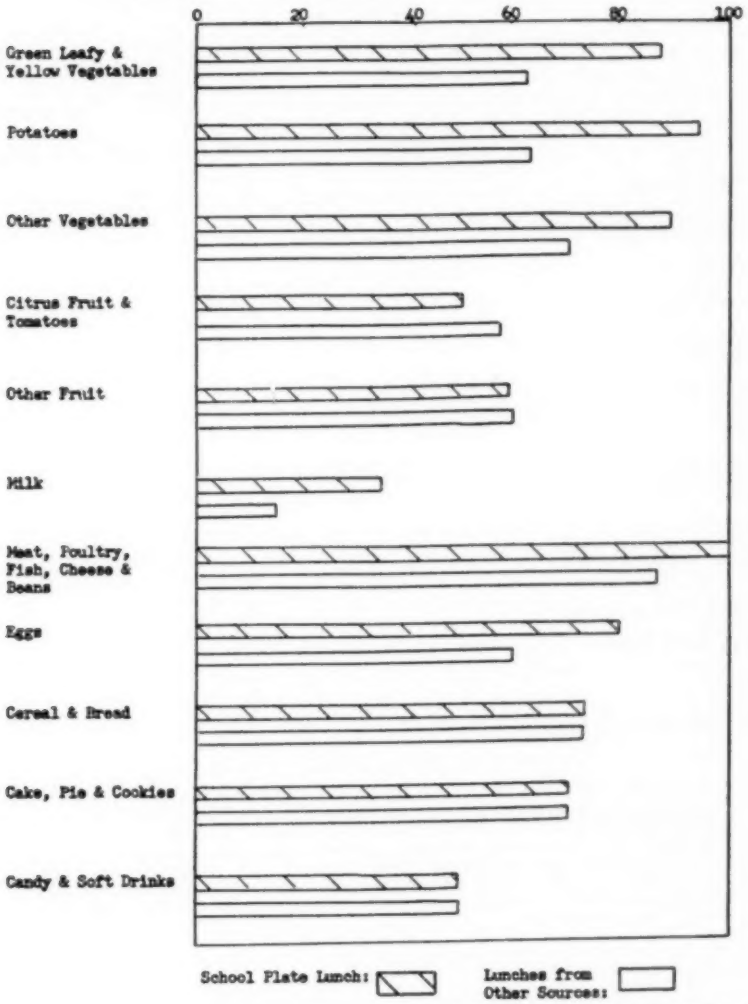
It is erroneous to presume that such brief observations would give accurate information or prove a basis to make generalities. However, some tendencies are noted. Evaluation of the three factors stated above were observed in the following manner:

Surveys from schools were checked against the daily food pattern for children from ages 10 to 12 years as suggested by the National Research Council.

FOOD GROUPS	AMOUNTS
Green leafy and yellow vegetables	1 serving
Potatoes	1 "
Other vegetables	1 "
Citrus fruit and tomatoes	1 "
Other fruits	1 "
Meat, poultry, fish, cheese, dried beans or peas	1 "
Milk	1 quart
Eggs	4-5 per week
Cereal and bread	2-3 servings
Butter or fortified margarine	1 tablespoon or more
Vitamin D	varies

Luxury foods, such as pie, cake, cookies, candy and soft drinks were noted.

CHART NO. 1
PERCENTAGE OF CHILDREN REPORTING ONE OR MORE SERVINGS OF THE ESSENTIAL AND LUXURY FOODS ON THE DAILY FOOD RECORD - ELEMENTARY SCHOOL



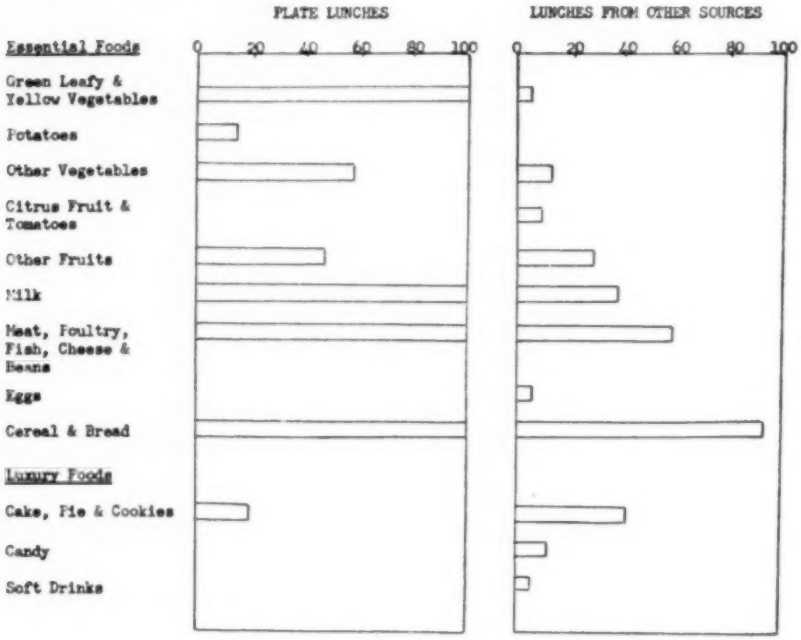
Similar results were obtained from a survey of 1,000 students' records at junior high school level.

There was little difference observed in the food value of the breakfast and supper of these students taking plate lunch versus those getting lunches elsewhere. (Frequently children who partici-

CHART NO. II

NUTRITIONAL CONTRIBUTION OF THE SCHOOL LUNCHES

Percentage of Children Taking One Serving of the Essential and Luxury Foods in Lunches



It is not assumed that the size of the portions of food consumed in this meal is always adequate to meet the daily food needs. However, with the exception of the citrus and tomato group and eggs, the plate lunch gave a greater contribution of the essential foods than lunches from other sources. From the menus observed it was felt that more vitamin C foods could be included in the school lunches, particularly fresh fruits and vegetables. This addition would also make the lunches more attractive.

The consumption of luxury foods was less with the children eating the plate lunch in the elementary schools.

pate in the school lunch program have better home diets.) With the exception of citrus fruits, the children selecting the plate lunch received from 10 to 30 per cent more of the essential foods than

the children securing lunches from other sources.

Foods in addition to school lunches were served in all school cafeterias. In the elementary schools only ice cream and cakes were available. In junior high and senior high schools the foods included were hot dogs, enchiladas, salads, pies, cakes, doughnuts, soft drinks and candy. Attempts are being made to gradually cut down on the sale of these less nutritious foods. Educational programs are carried out to help achieve this objective. This would follow along with recommendations of the Joint Committee on Health from the State Department of Education and State Department of Public Health, National Parent Teachers Association, American Medical Association and American Dental Association.

Concern over the high consumption of luxury foods can be justified for the following reasons:

(1) The intake of luxury food may crowd out foods necessary for growth and development.

(2) There is the possibility that these carbohydrate foods contribute to dental caries.

(3) A statement that children cannot afford plate lunches is not substantiated when money is spent for luxury foods. These foods give limited food value in proportion to their cost.

Educational Value. Brief observations give evidence of considerable nutrition education in the schools. In the elementary grades the science guides are excellent aids to the elementary grade school teacher in nutrition and health. Thus there is an opportunity for a child to learn why certain foods are needed for health and growth.

A little over a year ago a nutritionist was assigned to the school lunch staff. She plans and makes nutritional evaluations of menus. The nutritionist and school lunch coordinator from the San Francisco Unified Schools and the nutritionist and public health nurses from the Department of Public Health have all promoted nutrition education programs. This has been approached by participation in service health education classes for teachers, and serving as consultants to principals and teachers interested in nutrition projects. Nutrition projects have been carried out in about one-fourth of the schools in San Francisco. The school lunch program has been interpreted to parent groups, health educators, social workers and other community groups interested in the health of the child.

By promoting nutrition education and helping people realize that the school lunch is a good buy, these groups have stimulated a steady increase in the number of children eating in the cafeterias.

Elementary Schools. The elementary schools with cafeterias are serving nourishing food to children, and principals in these schools are interested and supporting the program. Opportunities to influence children of this age are great. At this early age participating in classroom activities, such as preparing and serving vegetables and eating in the school lunchroom with friends, helps children learn to enjoy a wide variety of wholesome foods. An educational school lunch program helps establish good attitudes toward healthful foods. It has been noted that students who go from elementary schools that have cafeterias to junior high schools have much better food habits than children from schools that do not have cafeterias. This indicates the value of the cafeterias at the elementary level.

The 24 cafeterias in elementary schools represent only about one-fourth of the elementary schools in the city. Cafeterias in new schools will be included. The additions of cafeterias to old schools should be seriously considered, particularly in areas where the economic level is low. The additional cafeterias would make it possible for more than just one-fourth of the grade school children to benefit from a plate lunch. Because children of this age gain most from this experience, it seems important that cafeterias be included in elementary school building plans.

Cafeterias are established in all junior and senior high schools. Their problem seems to be that of increasing the purchase of plate lunches and decreasing the sale of luxury foods.

Cafeterias at this level are supervised by teacher managers. These teachers are trained home economists, well prepared to supervise the preparation of foods, and, with administrative support, make the cafeteria a pleasant place to eat. In addition, these teachers have a science background to teach nutrition in their classes and answer requests to assist other teachers to incorporate nutrition into their classwork. This type of instruction teaches students the value of nutritious foods and the school lunchroom provides an opportunity to learn to enjoy body building foods.

Many activities have been carried out to increase the sale of plate lunches and make the lunchroom more comfortable:

(1) Sound-proofing of cafeterias and purchasing of much needed equipment has been helpful.

(2) Very small increases in the price of the lunch have been made, despite the rising cost of food and labor.

(3) Many educational programs, including feeding experiments, assembly programs and class work activities, have been carried out.

(4) The nutritionist from the Unified School District met with student groups in high schools to get student reactions to the cafeterias, constructive suggestions and menu ideas.

(5) The P.T.A. group at Balboa High School placed a juke box in the cafeteria. This increased the participation of the school lunch by making the cafeteria a social gathering place.

(6) The length of time students wait in line may discourage their eating in a cafeteria. Study of methods to speed up the food services are needed.

(7) The adjusting of school programs to give ample time for eating lunch would be helpful. Intramural sports and meetings at noon may interfere with the lunch program.

Some suggestions for further improvement in all the cafeterias would be to speed up the cafeteria service, to include more fresh vegetables and fruits to bring in more vitamin C, to continue to stimulate interest of parents, teachers and students. Possibly by soliciting students', teachers' and parents' opinions and setting up faculty and student school lunch committees, greater support could be obtained and more children would be eating the plate lunch. Also the addition of cafeterias would help increase the participation in the program.

SUMMARY

In the Spring of 1950, the nutritionist from the San Francisco Department of Public Health visited some 15 cafeterias and evaluated 200 food records. Since this date, the nutritionist has visited some 20 additional cafeterias. While these brief observations are no basis for making broad generalities, nevertheless, the following observations can be noted:

(1) Children taking the plate lunch had a more adequate daily food intake. Shown in Chart I.

(2) Children taking the plate lunch receive good contributions of 7 of the 11 essential foods while children eating lunches from

other sources receive a smaller contribution representing only 4 of the group of 11 essential foods. (Chart II) Children eating lunches in the cafeterias in the elementary schools consumed less luxury foods, such as cake, pie, cookies, jelly, candy and soft drinks.

In elementary school cafeterias only cake and ice cream are served. In the junior and senior high schools they include enchiladas, salads, hot dogs, pies, cakes, doughnuts, soft drinks and candy. Attempts are being made through educational programs to gradually reduce the sale of less nutritious foods. Chocolate milk has been deleted from school lunch menus.

Because changes take place slowly, objectives are set on a long term basis.

By establishing the cafeterias under the centralized management of the coordinator of school lunches and home economics, and adding a nutritionist to the staff, many advantages are possible, including not only higher food standards but the coordination of classroom activities with the school lunch program.

The nutritionist and the school lunch coordinator, principals and teachers from the San Francisco Unified School District, work with the nutritionist and public health nurses from the Department of Public Health, educators in teacher training schools interpreting the objectives of the school lunch program, and promoting better nutrition in the community.

With greater emphasis being placed on health education, medical and education authorities and parent groups are realizing the importance of an educational school lunch program supported by nutrition instruction in the classroom. These are the best ways of influencing children's food habits and thus contributing to better growth and development of our school children. For this reason the school lunch program should be an integral part of the health program.

The school lunch program needs more emphasis, publicity and recognition for its valuable contribution. A beginning has been made in some schools of interesing parents, students and teachers in the purposes of school lunch. This work needs to be continued and expanded, so that a greater percentage of the school children are receiving the advantages of the school lunch.

In California, in the past five or six years, the number of schools participating in the national school lunch program has

almost tripled. Thus the funds have been dispersed more widely. However, the reimbursement for school lunches has been cut from nine cents to four cents. With the decrease in reimbursement and an increase in food and labor costs, the school lunch program is facing difficult problems. This brings need for continued nutrition education programs in the school and community interest and support in the school lunch programs.

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ACUTE LARYNGOTRACHEOBRONCHITIS IN CHILDREN. (Ugeskrift for Laeger, Copenhagen, 113: 885, July 5, 1951). Siemssen asserts that acute nonspecific laryngotracheobronchitis in children is not well enough known. He attributes to it a number of unexplained deaths in children and cases erroneously diagnosed as primary pulmonary affections. It is defined as a symptom complex depending on an infectious nonspecific, probably virogenic, descending stenosing process in larynx and the lower respiratory passages. In acute cases suffocation is the immediate danger. When the course is more protracted, hyperpyrexia and shock threaten as a general reaction to the infection. Pulmonary complications aggravate the prognosis. The disorder is a grave complication in epidemic subglottal pseudocroup. It sometimes, not often, appears as a complication in acute contagious diseases of children. Attention is called to the peculiar regression from laryngeal stridulous dyspnea to superficial tracheobronchial dyspnea without stridor on spread of the stenosing process to the lower respiratory passages. Four cases are presented in detail. With the present day chemotherapy, treatment is now attempted along conservative lines. The necessity for careful observation and readiness for possible endoscopic surgical intervention is stressed. The cooperation of practitioners, internists, or pediatricians and otolaryngologists is important.—*Journal A.M.A.*

CLINICAL REVIEW

In order to encourage the writing of clinical articles by recent graduates or senior medical students, the ARCHIVES *will publish monthly at least one such paper from the classes of Doctor Reuel A. Benson, New York Medical College, New York, and Doctor Philip Moen Stimson, Cornell Medical School, New York. Other interested medical schools are cordially invited to submit student papers for consideration.*

ACUTE GLOMERULONEPHRITIS*
WITH SPECIAL REFERENCE TO ETIOLOGY

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New York.

Acute glomerulonephritis may be defined as an acute inflammatory reaction, primarily of the kidney glomerulus, characterized clinically by hematuria, cylindruria and albuminuria, with or without edema, hypertension, cardiac failure, lowered renal function and nitrogen retention. The correlation of albuminuria with kidney disease was first noted in 1827 by Richard Bright. Since then the nomenclature of "Bright's disease" has become quite complex and often contradictory. Acute glomerulonephritis has been described also as acute interstitial nephritis, acute parenchymatous nephritis, acute diffuse nephritis, and all possible permutations of these four. Its existence as a single disease entity has been introduced, denied and defended. Some workers[11] consider almost any type of renal damage to be a part of glomerulonephritis; others believe glomerulonephritis to be a generalized disease of the capillaries.[5] Here we shall defend the concept that acute glomerulonephritis is a distinct disease entity with a definite etiology, course and prognosis.

Clinical Aspects. Acute glomerulonephritis is primarily a disease of childhood, 40 per cent of 600 cases occurring in the first decade[26, 51, 60] and 80 per cent before the age of 30 (96 per cent before age 50). According to most surveys, there is a male to female ratio of 2:1. It has been shown[60] that there is a seasonal variation in the North (New York) not found in the Southern United States, i.e., increased prevalence in the winter with a sharp drop in the summer time. The yearly incidence, however, is quite

*Student Thesis, New York Hospital–Cornell Medical Center, New York City.

similar, 5 per 1000 hospital admissions (0.62 per cent in New York, 0.47 per cent in the South).

The disease is manifested by five clinical syndromes[31]: (1) the urinary, (2) hypertension, (3) edema, (4) nitrogen retention, and (5) uremia, the only one constantly present being the urinary which is characterized by hematuria, cylindruria, albuminuria and increased cellular excretion. Almost pathognomic is the mixed blood and cellular cast.[1] The urine is best followed by means of the Addis count[1] on fresh, concentrated, acid specimens to avoid lysis of formed elements. The hematuria may be gross or microscopic; in the former case often appearing like coffee, due to acid hematin. Other signs referable to cardiovascular damage, such as electrocardiogram changes, cardiac dilatation, retinopathies, and cerebral ischemia or edema, may be present. Edema in most instances is minimal, being manifest in the morning by a slight puffiness of the lids. Fever, especially in severe cases, may be marked. Symptoms vary from slight lassitude to marked malaise with prostration and vomiting. Some show convulsions and coma. It is important to note that a patient may have a full-blown attack without any subjective awareness of illness.

The laboratory findings in acute glomerulonephritis, other than the urine, are in general nonspecific. There may be a low-grade normochromic anemia, a slight to moderate to severe elevation of the blood urea nitrogen, and increased sedimentation rate.[30] This last is a valuable prognostic sign, for as long as the rate is abnormally rapid, the disease must be considered active. Addis[1] considers an elevated blood creatinine to be the most important single chemical determination in the diagnosis of glomerulonephritis. However, diminished renal function is usually not evident, and very rarely marked, unless the case is progressing toward uremia. In the more severe cases, hypoproteinemia, decreased albumin-globulin ratio and lipemia may be present, although these are more commonly seen in chronic glomerulonephritis.

The sudden outpouring of blood, cells and casts which marks the onset of acute glomerulonephritis initiates a disease process which is essentially reparative[1] to the initial injury, i.e., the course of the disease depends upon the extent and duration of the initial injury and the compensatory power of the kidney. In most instances these signs disappear in from one to three weeks. The last

to return to normal is usually the Addis count, which may remain abnormal even up to a year[1] and still allow for complete recovery. Usually, however, an abnormal count persisting for more than a few months connotes a poor prognosis. The mortality in the acute stage is low, averaging 5 to 10 per cent.[1, 26, 45, 55, 58] More children than adults have a complete recovery. The general mortality, including chronic glomerulonephritis, ranges from 10 to 85 per cent,[37] varying directly with the age at onset.[58] The chief causes of death are uremia, cardiac failure and intercurrent infections. In the fatal cases of acute glomerulonephritis we also find the cases of "subacute glomerulonephritis," so-called because the patient succumbs in a matter of months rather than weeks or days. The pathological *sine qua non* for this stage is the presence of epithelial crescents in Bowman's capsule. There is little reason to consider this more than a "late" acute glomerulonephritis.

The disease itself may disappear, remain latent for a time or progress into a degenerative phase ending in uremia and death. In the latent phase we find a persistence of the urinary findings and in these patients the eventual prognosis is usually grave, although they may be asymptomatic for years. In occasional cases there may be complete recovery from this stage. Murphy[50] cites the following as criteria of the transitional (or latent) phase: mild anemia, diastolic blood pressure above 90 mm., persistent albuminuria (with or without erythrocytes), a high sedimentation rate, and normal renal function, save that the urea clearance is usually impaired. This is the group which terminates in chronic glomerulonephritis.

Pathophysiological Aspects of Acute Glomerulonephritis. The fully developed lesions of acute glomerulonephritis are well-known, with the pale, edematous kidney showing petechial hemorrhages and large cellular glomeruli. An excellent review of the pathological findings to 1929 may be found in McGregor's paper.[48] He himself was the first to describe the intracapillary hyaline fibers which are generally assumed[5, 9, 20] to represent an irreversible stage and the first step in the hyalinization of the glomeruli. McGregor claims that "very early in nephritis there is a complete cytoplasmic wall [of proliferated endothelium] lining the loops" and that "the earliest intracapillary changes are accompanied by proliferation of the epithelium." MacCallum[43] claims that these intracapillary

fibrils actually arise from the intercapillary connective tissue which he showed to be increased in acute glomerulonephritis. Baehr[5] considers the capillary endothelial swelling to be the basic lesion, but it must be admitted that both swelling and proliferation occur in glomerulonephritis. Dunn[20] considers the earliest lesion to be a "uniform capillary dilatation" with a secondary endothelial swelling and proliferation, and later the formation of the intracapillary fibrils. A note must be made about the early changes of glomerulonephritis as put forth by Bell.[3] He described various proliferative changes and laid great stress upon the fragmentation of the basement membrane, upon the basis of which changes he described a "sub-clinical" glomerulonephritis found in a number of other infectious and noninfectious conditions. On the basis of such findings he claims that glomerulonephritis ". . . is not caused by a specific etiological agent . . ." but is a response to any soluble toxic substance. In other words, A (early changes) is found in B (glomerulonephritis) and A is found in C (other conditions); therefore B is C (glomerulonephritis is a non-specific condition). The logical fallacy is obvious.

We may explain our urinary findings in acute glomerulonephritis by increased glomerular permeability and tubular sloughing. The latter can be explained on the basis of a relative anoxia due to ischemia. Since the tubular blood passes through the glomerulus before reaching the peritubular plexus, we may say that, according to Dunn's hypothesis, the blood flow is first slowed by the dilatation and secondarily lessened by the proliferation. There may also be some cortical by-passing due to the juxtamedullary shunts of Trueta. Goldring,[22] on the basis of phenol red (P.S.P.) and insulin clearances, posits an initial transitory hyperemic phase before the ischemic period develops. That kidney function continues relatively unaltered in so many cases of glomerulonephritis is probably due to the rapid regenerative power of the tubule cells along with reversal or lessening of the ischemia. There is also some evidence for the development of shunts from the afferent arteriole to the peritubular plexus; such shunts (Ludwig's vessels) have been demonstrated by Oliver[52] in cases of chronic glomerulonephritis.

Increased permeability of the glomerular capillaries is a necessary fact attested to by the urinary findings. It has also been demonstrated by dye studies by Toynbee and Thoma[48] as well as by

Oliver.[52] Dunn ascribes it in part to the lessened blood flow which, according to Bernoulli's theorem, produces an increase in filtration pressure. Doubtless the structural alterations seen also indicate the functional alteration of increased permeability. The moderate suppression of urinary volume, which is usually found, also may be due to reduced blood flow which, although it would tend to raise the glomerular filtration rate toward normal, might allow for more complete reabsorption by the still-functioning tubules. This would tend to produce hydremia (and edema); Addis[1] refers to Cardozo's findings of hydremia in 16 of 18 patients with acute glomerulonephritis in support of such a view.

The edema of acute glomerulonephritis is due to several factors, one of which is the protein loss. Addis[1] claims that there is also a qualitative change in the protein produced by the tubule cells during reabsorption from the glomerular filtrate. The hydremia referred to above may also play a role. Sodium retention does not seem to play the role here that it does in the cardiac and chronic nephritic dropsies. The hypertension found has also been implicated in the production of the edema. In general, the protein content of the edema fluid is low, thus favoring factors other than capillary permeability. The predilection of the fluid for the eyelids has been explained on the basis of the distensibility of these tissues and hence an inability to raise the tissue pressure sufficient to prevent the excess fluid retention.

The hypertension may be due to the "renin mechanism" secondary to renal ischemia. It is usually relieved by vasodilators such as magnesium sulfate. Arnott and Matthew[4] implicate neurogenic vasoconstriction, reserving for the chronic phase of the disease a humoral role in the etiology of hypertension. The heart failure in acute glomerulonephritis has received no really adequate explanation.

Nitrogen and creatinine retention, as well as the uremia, are chiefly explicable on the basis of diminished tubular function in selective reabsorption, as well as lessened glomerular filtration rate. The lipemia, found more often in the chronic phase, is considered the result of absolute increase in the blood lipids as well as diminished plasma proteins, which Addis[1] feels serve to "coat" the fat molecules in the normal.

Differential Diagnosis of Acute Glomerulonephritis. There are a number of other conditions which may be confused clinically or

even pathologically with this disease. These may be classed as (1) primary renal diseases, (2) secondary renal diseases, (3) chemical and deficiency nephropathies, and (4) non-renal conditions.

The first group would include (a) lipoid nephrosis—a purely degenerative lesion almost exclusively of the tubule, and characterized by great albuminuria, massive edema, low plasma proteins and hypercholesterolemia; (b) Kimmelsteil-Wilson's interstitial nephropathy[36] is ascribed to "a hyperergic reaction to bacteria and their toxins" and is noteworthy for the lack of involvement of the glomerulus; (c) amyloidosis must also be considered along with renal tuberculosis and neoplasms; (d) polycystic kidneys may give a clinical picture impossible to differentiate from acute glomerulonephritis.

Secondary renal diseases include: (a) arteriolonephrosclerosis; (b) focal embolic nephritis—due most often to Strep. veridans emboli[56, 8] in cases of subacute bacterial endocarditis, though Gross[30] describes a focal glomerulitis in elderly patients which he considers due to loss of kidney substance with "overworking" of the remainder; (c) disseminated lupus erythematosus, although Stickney and Keith[66] found no pathognomic lesion, will produce a glomerulitis; (d) the toxemias of pregnancy; (e) yellow fever,[24] typhus[79] and several other rickettsial diseases[3] also produce renal lesions.

Uranium, mercury and dichromate, as well as the sulfas, will give renal damage clinically similar to acute glomerulonephritis. Experimental acute choline deficiency[28, 29] and hypovitaminosis A with hypervitaminosis D[53] will also produce renal insufficiency.

Pepper[54] reported a case with fixed low specific gravity, abnormal Addis count, blood urea nitrogen of 30 mg.%, and a urea clearance of 20 per cent—all reversed by the removal of a parathyroid adenoma. The "shock kidney"[18, 40] is also a well-known cause of renal failure.

All these conditions may, more or less, give a picture difficult to distinguish from acute glomerulonephritis and should be kept in mind when confronted with such a diagnosis.

Chronic Glomerulonephritis. This is a stage of glomerulonephritis marked by albuminuria, cylindruria, edema and elevated blood pressure. The laboratory findings include normochromic or hypochromic anemia, hypoproteinemia, increased sedimentation rate, and signs of decreased renal function. The chronic nephritic may

revert to the latent stage, but this in any case is only temporary, unless death occurs from an intercurrent infection.

The chronic stage, although progressive, may be marked by exacerbations and remissions. The exacerbations are most commonly induced by conditions which may precede the initial (acute) stage, i.e., hemolytic Strep. infections[61] although the "incubation period" is considerably shorter (1-4 days). However, any stress, such as puberty, parturition, other infections, may also cause a recrudescence of the disease, possibly by means of an anamnestic reaction.[1] After each exacerbation there is usually further diminution of renal function.[61]

To sum up the laboratory findings in a progressive chronic glomerulonephritis, the serum protein is depressed, the albumin globulin ratio tends toward inversion, and there is nitrogen retention leading to uremia, with an elevated serum creatinine. Hyperlipemia, involving all the lipids, may be present, although the cholesterol drops terminally toward normal. There is sulfur and phosphorus retention; the serum and cerebrospinal fluid calcium are low. Anemia, acidosis and achlorhydria are common. Kidney function is progressively diminished; urea clearance falls toward zero terminally. Albuminuria and cholesteroluria are marked. Hematuria is variably and inconstantly present. The edema, which has been marked throughout the chronic phase, disappears when the compensatory powers of the kidneys have been exhausted, and is a sign of impending death. In this terminal phase the urine is very dilute with a high protein content and many broad "renal failure" casts. Death, as in the acute phase, is from uremia or secondary infection, or (less commonly) from cardiac failure. Intercurrent infections are extremely common due to the debilitated state, and to the decreased gamma globulins[1] which fall in the hypoproteinemic patient.

The typical pathological findings in chronic glomerulonephritis are the "small, firm, contracted, granular kidneys" with hyalinized glomeruli, atrophied tubules and interstitial fibrosis. Compensatory hypertrophy, especially of the proximal convoluted tubule,[1, 47, 52] is evident in the intact nephrons, with the presence of occasional aglomerular tubules. This picture is given chiefly by chronic glomerulonephritis and malignant nephrosclerosis, with an intermediate called by Horn[33] "accelerated chronic glomerulonephritis."

The pathological picture it should be emphasized is *not* definitive, and may be the result of almost any chronic renal disease.

A word may be said about the "nephrotic stage of nephritis." This is a clinical designation referring to the presence of the "nephrotic syndrome" and consists essentially of edema and albuminuria without hematuria. This is supposed to indicate a predominantly tubular (nephrotic) lesion. It is our opinion that this term adds little nosologically; true nephrosis may simulate chronic glomerulonephritis clinically.

Management of Glomerulonephritis. Symptomatic relief is all that can be offered at this time for this disease. Even the adrenal hormones have so far been without avail.[31] Cardiac failure is treated no differently here than elsewhere. Our aim is to have the kidney perform as little work as possible; the chief alterable functions of the kidney are (1) osmotic work, (2) work in acid-base balance, and (3) work in selective reabsorption. The first is minimized, according to Addis,[1] by diuresis, best produced by a high fluid intake. The second is lessened by a low base intake; in fact, it is minimal when the patient is in acidosis. Selective reabsorption includes the retention of electrolytes, glucose and products of protein metabolism, taking place chiefly in the proximal tubule. Addis has found that increasing the protein intake of rats will lead to an increase of kidney protein (as a measure of kidney size) to 60 per cent above normal. Such a result also occurs after unilateral nephrectomy, and further, this "compensation hypertrophy" and "work hypertrophy" are additive. Rats lacking three-quarters of the renal parenchyma were consistently killed by renal failure on high protein diets.[1] Oliver has shown that these hypertrophic changes take place chiefly in the proximal convoluted tubule, as is also the case in human chronic nephritis.[32] Kempner showed clinical improvement in more than half of his patients with chronic primary kidney disease for periods up to 32 months on his rice diets.[35] Therefore, to reduce kidney work, one should have a minimal protein intake (0.5-0.7 grams per kilogram of body weight per day beyond replacement of renal losses), salt should be restricted, and fluids given ad lib.

Human Evidence on the Etiology of Acute Glomerulonephritis. It has been noted for over a century that acute glomerulonephritis follows almost invariably an infection, and that this infection is

most often clinically absent when the onset of nephritis is noted. One of the few points that has the universal agreement of workers in this field is that bacteria cannot be demonstrated in the glomeruli of patients dying of glomerulonephritis, regardless of the amount of time that has elapsed since the onset of the disease.

The nature of the infection which precdes acute glomerulonephritis has received much attention. Folkers[26] found half of his cases to follow upper respiratory infections; Volhard and Fahr[69] considered three-quarters as upper respiratory infection; Longcope,[38, 39] 80 per cent upper respiratory infection; Addis[1] found 78 per cent due to upper respiratory infection; Matthew[47] found about 70 per cent due to upper respiratory infection. In Rudebeck's series,[58] although no figures were given, the predominating infection was considered to be of the upper respiratory tract. Seegal,[60] too, quoted the prevalence of upper respiratory infection. Therefore, we may say that upper respiratory infections, especially tonsillitis and sore throat, but including scarlatina, sinusitis, bronchitis and otitis media, are found to precede about three-quarters of some 1,700 cases of acute glomerulonephritis. Figures for the absence of any previous infection vary from zero[58] to 13 per cent[38]; however, it should be considered that many patients will not recall a sore throat or "cold" even when specifically questioned. It seems safe then to conclude that in the vast majority of cases an infection, usually of the upper respiratory tract, antedates the onset of acute glomerulonephritis, by a period ranging from one to three weeks.[47] This relationship between infection and glomerulonephritis is too constantly seen to be mere coincidence; it seems valid to say that it plays some role in the causation of acute glomerulonephritis, and that, for the moment, is as far as we may go.

The next point to be considered is the bacteriology of these infections. Most of the workers cited above noted that these infections, or those other than respiratory which were involved, are conditions usually caused by beta-hemolytic streptococci, but the data given in support of this conclusion are rather sparse. Longcope[39] found beta strep. to be the predominating organisms in the throats of 69 per cent of his cases, with alpha strep. in an additional 12 per cent. A further study by the same worker showed beta strep. to predominate in 58 per cent and alpha strep. in 13 cent of the throat cultures examined. However, the difficulties in

such a procedure are apparent: first, the clinical evidence of infection has usually disappeared by the time that glomerulonephritis has begun, and therefore it is likely that the bacteria may also be gone; second, beta-hemolytic strep. may be found in the throats of normal "carriers," though probably not as the predominating organism; third, the culturing of throat flora is obviously only of value in throat infections. To exemplify the inaccuracies manifest in this procedure, consider that Longcope[38] found beta strep. in only two of four cases of scarlatina, a proven Strep. infection.

The most definitive study on the relationship of strep. infections to acute glomerulonephritis has been that of Lyttle et al.[42] They tested the sera of 116 unselected consecutive patients with clinical acute glomerulonephritis and found incontrovertible evidence of recent beta-hemolytic streptococcal infection in 94 per cent. Of the remaining 6 per cent, one patient had pneumococcal pneumonia three weeks prior to the attack of glomerulonephritis, one had no evidence of any infection, and the remaining five showed absolute or probable evidence of recent hemolytic strep. infection. This was done by means of the antistreptolysin titer, which is a measure of the antibody produced in response to streptolysin (hemolysin) from beta strep. Streptolysin-O (streptolysin-S does not rise above 60 units) is produced by group A, C and G (large colony) beta-hemolytic strep., and "the antistreptolysin titer in individuals who have been free of hemolytic streptococcal infections is less than 100 units."[42] The titer in Strep. infections reaches a maximum level two to three weeks after infection. Lyttle's standard for infection was 125 units (as well as progressive changes in level). They found that in acute glomerulonephritis the titer was maximal at the onset or during the first few weeks after onset, and started to fall during the first or second month of the nephritis. The height of the antibody titer was not correlated with any clinical manifestation of glomerulonephritis. In their series only 72 per cent of the patients had had a recognized prodromal hemolytic streptococcal infection. Here then we have as absolute proof as can be obtained that the preceding infection in acute glomerulonephritis is almost invariably due to beta-hemolytic streptococci.

Since it is known that scarlet fever is definitely due to beta strep., let us consider more fully the relation of this infection and acute glomerulonephritis. Bright[14] wrote that ". . . scarlatina

has apparently laid the foundation for the future mischief." From that time on the sequence was so commonly seen that acute glomerulonephritis was called postscarlatinal nephritis. Longcope[38] found 16 per cent of complications of scarlet fever were acute glomerulonephritis. But it has been argued, quite validly, that acute glomerulonephritis is rather rare, whereas hemolytic strep. infections are common. For instance, only 1 per cent or so[1] of scarlatinals come down with a clinically diagnosed attack of acute glomerulonephritis. If hemolytic strep. cause, in some fashion, our disease, it should be more in evidence than in one of 100 patients. This argument may be refuted by the familiar appeal to constitutional factors (unprovable) or to heredity. The only evidence we have found in this respect is Addis'[1] account of four sets of identical twins, one of which in each pair had acute glomerulonephritis, but in every case the other twin was free of the disease.

However, there is also the well-known concept of subclinical infection, i.e., that a person may be infected with an organism but show no outward (clinical) evidence that such is the case. Obviously we can not use our serology, such as may be employed in a number of other conditions. But it is known that the only finding that is constantly present in clinical glomerulonephritis is the urinary syndrome.[51] Should we find any urinary evidence of a mild attack of acute glomerulonephritis, in the absence of all other infections, and occurring soon after a hemolytic strep. infection, our case would be well supported. Actually this proof, if found, would put the condition almost into clinical glomerulonephritis, and we could safely posit a continuation of the disease-spectrum—from urinary plus other signs to urinary alone to no signs. Such a test was done in 1933 by Lyttle,[41] using the Addis sediment count in scarlet fever patients. He performed these on 14 males from 4 to 14 years of age, three times a week for periods up to 45 days after the onset of scarlatina. It must be noted that ". . . *no* cases of postscarlatinal nephritis have been included . . .", and *no* patient developed any of the typical signs or symptoms of nephritis. The patients were on low-protein, low-salt diets and bed rest. The temperature of 12 patients was normal by the sixth day, the other two by the ninth and twelfth days. Lyttle states that ". . . all cases showed moderate transient increases in the excretion of protein, cells [including erythrocytes] and casts in the urine dur-

ing the period from 8 to 45 days after the onset of scarlet fever." These increases were in all cases well above the normal limits as described by Addis,[1] and were irregular and explosive in character. This we believe adequately answers the objection above.

There are a few other bacteria which seem to induce acute diffuse glomerulonephritis. Lyttle,[42] Matthew,[47] Seegal[60] and Longcope[38] reported such cases after pneumonia due to the pneumococcus. Bell[5] mentioned glomerular lesions in different endocarditides, the predominating one being subacute bacterial endocarditis, in which he found diffuse glomerular lesions in 65 per cent and similar focal lesions in 53 per cent of the cases. Baehr[6] made the interesting discovery that bacteremic subacute bacterial endocarditis patients do not get glomerular lesions, but that, of 53 patients recovering from subacute bacterial endocarditis—and bacteria-free—19 died of "diffuse glomerulonephritis with uremia." That most of Bell's cases are focal embolic nephritis seems probable, but Baehr's appear, in some cases anyhow, to be diffuse; however, 18 of the 19 died in the subacute or chronic stages, which may easily have been due to focal embolic lesions. Rigdon[52] reported seven cases of Staph. aureus infection with clinical findings ". . . the same as those in any case of acute glomerulonephritis . . ."; the lesions were diffuse *or* focal, and he likened them to "Baehr's subacute bacterial endocarditis kidney thrombi." It seems that Strep. viridans or Staph. aureus lesions, while usually producing focal embolic nephritis, may in rare instances produce a true acute (diffuse) glomerulonephritis.

One other facet of the human evidence remains to be mentioned. Thomson et al.[68] studied the serum complement level in 18 patients with acute glomerulonephritis, 33 patients with pre-eclampsia, and 157 (normal) pregnancy controls. In 16 of the 18 nephritic patients they noted a reduction of the normal complement level to far below normal; "in many cases there was apparently no complement present at all." None of the other persons tested had any reduction of complement. What this means is at present unknown. At least it would serve to differentiate acute glomerulonephritis from toxemias in the pregnant patient. The functions of complement *in vivo* are unknown; *in vitro* it forms a component of antibody reactions. Further work on this point is most strongly indicated.

Any hypothesis as to the etiology of acute glomerulonephritis will have to take into account all these factors. Acute glomerulonephritis is due to beta strep., but only in their absence. Therefore it is due to some product of these bacteria, which may be called a soluble toxin, for want of a better name; soluble, since the site of infection plays little role in the production of the disease. It must also be a substance that has a specific effect on the kidney, since the vast majority of observers find no primary extrarenal damage. In addition the disease appears when antibody formation to the previous infection is at its height. The role of complement herein is so far unknown.

Experimental Nephritides. Throughout the twentieth century workers have been attempting to reproduce this disease in laboratory animals. The early work consisted in the injection of living or dead Strep. viridans bacteria.[12, 13, 32, 56] The glomerular lesions so produced were either definitely focal in nature, or so obfuscated by chronic changes that their character could not be adequately determined. Some of the workers[32] claimed their cases to be "diffuse glomerulonephritis," but offered no adequate pictorial proof thereof. That these nephritides were not the animal counterpart of acute glomerulonephritis seems probable, and work in this vein was soon dropped.

Instead, more attention was paid to the beta-hemolytic group. Lukens[16] produced a glomerulitis by injecting killed Strep. intraarterially into rabbits but this too appeared to be focal embolic nephritis, despite the absence of bacteria. Dick and Leiter[19] produced amyloidosis in the kidney of 7 of 8 rabbits with hemolytic Streptococci from the throat of a patient with acute glomerulonephritis. Were a Congo red stain not done these might well have been called subacute glomerulonephritis, the chief clinical difference being the absence of hematuria. The import of this finding is unknown; we have found no similar report. It is of interest that in these animals the liver was uninvolved, and the spleen showed but minimal amounts.

More orthodox results were obtained by Duval and Hubbard.[21] They found ". . . experimentally induced nephritic lesions which are analogous in kind and variety to those of acute scarlatinal nephritis in man. . . ." They used immunized (to Strep. scarlatinae) rabbits which they injected with "lysate," a substance prepared by intraperitoneal injection of homologous organisms into

other immunized rabbits, with collection of their peritoneal fluid in two to three hours. This fluid was sterile on culture and had a lethal dose of 1 ml. Their conclusion was that the products of the antigen-antibody reaction of an immunized host with Strep. will cause kidney lesions, but only in similarly immunized animals. That these lesions are those of human glomerulonephritis has been questioned.

The next important bit of work was done by Masugi.[44, 45, 46] He developed the procedure, based on the work of Lindemann in 1900, of producing organ-specific antisera. His method involved the injection of rabbit kidney perfusate intraperitoneally into Peking ducks for 18 to 30 injections. The blood serum of these ducks was heat inactivated and then injected intravenously into rabbits in doses of 5 to 15 cc. His conclusions were ". . . dass es sich hier um eine ausschlaggebende Rolle spielt" and ". . . dass es sich hier um eine hyperergische Reaktion der Niere gegen irgendein Eiweissantigen handelt." He found the clinical course and pathological lesions strikingly similar to those of human acute glomerulonephritis. He claimed the infection produced was diffuse, though it must be affirmed that in some of his microphotographs the changes seemed to be more of a focal nature. Be that as it may, this was the experiment *de rigueur* in the late 30's, and innumerable reports were written in which this work was emulated.

In 1936, Smadel and cohorts presented a series of papers dealing with a number of aspects of Masugi's "nephrotoxic nephritis," as it had come to be called. They showed[62] that nephrotoxin (produced in rabbits by rat kidney injections) is a relatively organ-specific antiserum which has two different actions: the first is a generalized anaphylactoid, with hematuria present; the second is the true nephrotoxic, without hematuria. They found that the serum of such nephritic rats will not produce similar nephritis in other rats, i.e., the antiserum has been completely absorbed or destroyed; that the antiserum can be absorbed with fat-free kidney extracts; and that nephrotoxin is present in the globulin fraction. The clinical studies[64] are typical of what one would find in an unselected group of human glomerulonephritis cases: variation from death to almost no injury.

However, the pathological findings[63] are not quite so encouraging. The glomeruli were large and anemic, due to swelling and thickening of the glomerular intercapillary substance; the tubules

showed minor degenerative changes. But proliferation of the glomerular endothelium in the acute cases "has occurred only occasionally," and then "only after massive doses of anti-kidney serum." The lesions of chronic nephrotoxic nephritis[65] were more similar to human chronic glomerulonephritis, and also less useful for comparison because of the relative non-specificity of such changes.

If saline extract of perfused rat kidney is injected into the rats just prior to the injection of the nephrotoxin, the renal damage is prevented.[67] No other substance will act in this fashion, though liver will also neutralize the antibody *in vitro*. They have also shown a difference in the reaction to this nephrotoxin manifested by three strains of rats; the homologous strain was most susceptible and showed somewhat more severe lesions than the others.

Ahlström,[2] in a similar experiment, stated that "bei Kombination einer kleineren Toxindosis mit wiederholten Seruminjektionen zeigten die Nieren . . . die Veränderungen . . . stets diffus. . . ." His conclusion was that "die proliferativen Glomerulusveränderungen erinnern an die Glomerulusbilder bei der akuten diffusen Glomerulonephritis des Menschen."

Ehrich,[22] using Masugi's method, produced a focal glomerulonephritis, with a clinical picture of acute glomerulonephritis (except for hematuria) with a single injection of the serum into healthy rabbits. He therefore claimed it could not be an allergic phenomenon, but was rather toxic in nature. However, the reasoning is rather thin, since kidney antibody could react with normal kidney (antigen) even though the animal were not previously sensitized. A later paper[23] by the same author, using Masugi's method, showed a picture much more similar to human glomerulonephritis; there was a transitory diuresis, followed by oliguria, decreased filtration, hematuria, albuminuria, edema and elevated blood urea nitrogen. The pathological picture after one week was that of enlarged, pale, petechial kidneys with tufts markedly enlarged due to cellular proliferation, in all cases. Half also had fibrin deposits in the capsular space. Another study by Ehrich et al.[24] substantiated these findings, and also showed the presence of an initial phase of glomerular hyperemia, followed by ischemia. The picture here is almost identical with human glomerulonephritis.

The logical next step was to combine the nephrotoxin and the bacterial toxin. Such a study was done by Schwentker and Comploier.[59] It was found that when rabbit kidney plus Strep. or Staph. toxins were injected into rabbits, their sera produced complement fixation with rabbit kidney emulsion as antigen, and in fairly high titers. Serum after kidney injection alone gave no results; the serum after bacterial toxins did give such an antibody-antigen reaction, but in low titer. It was also shown by absorption studies that this antibody consisted of two components: one was organ (kidney) specific, the other was not.

One important finding of their study was the action of *human* sera on *rabbit* kidney antigens. *92 per cent* of scarlatinal patients had sera which gave positive complement fixation reactions with rabbit kidney as antigen; only 10 per cent of the normal controls gave a similar result. The titers were evenly spread from + to ++++. Only 2 per cent gave any reaction with rabbit brain as antigen. This shows that such patients have an organ specific but not species specific antibody in their sera. That the reaction is not due to the Strep. toxin alone is indicated by the very low titers which such toxins had given in the first part of their paper. In all respects the reaction is identical with that produced by sera after the antigenic action of Strep. toxin plus kidney injections. Now scarlatinals *do* have Strep. toxins in their blood. They have also been shown, in the first part of this paper, to produce *some* glomerular injury in *all* cases.[41] In other words, we have patients with subclinical glomerulonephritis giving an antibody-antigen reaction as if they had *kidney antibodies* in their sera—or a Strep. toxin-kidney complex which acts as an antibody for *heterologous* kidney.

For the moment we shall consider further experimental evidence. Fouts et al.,[25] with hen anti-dog-kidney serum produced nephrotoxic nephritis in all of six dogs. Six to ten days after the injection there was an acute phase characterized by hematuria, proteinemia, anorexia, increased renal blood flow and decreased glomerular filtration rate. Then the renal flow was decreased, with a much lessened renal clearance. The filtration rate was still proportionately more reduced, as shown by the phenol-red-clearance to inulin-clearance ratio, which was elevated. No pathological studies were done.

Cavelti and Cavelti gave us the next extensive study of nephrotoxic nephritis. By means of collodion agglutination of rabbit kidney (antigen) with antibodies, they showed that only a mixture of Streptococci plus rabbit kidney, when injected in rats, produced such agglutinable antibodies.[15] No strain of Strep. or Staph. alone, nor plain kidney so injected formed such an antibody. The highest titers were found after the injection of whole killed Strep. and rabbit kidney. With repeated injections of Strep.-rat kidney mixture into rats[16] they obtained a high percentage of changes, characterized clinically by proteinuria, cylindruria, hematuria, increased renal cell excretion with some leukocytes—showing "histologically definite glomerular lesions." In many cases these signs disappeared in from two to eight weeks; in some they persisted with a terminal increase in proteinuria.

As evidence for their viewpoint that kidney antibodies were responsible for the production of these lesions, they stated that: (1) there is always a time-interval of one to two weeks between immunization and the appearance of urinary symptoms; (2) "there was some, although by no means complete, correlation between the presence of antibodies to kidney as demonstrated *in vitro* and the development of nephritis." The lack of absolute correlation they lay to the fact that such kidney antibodies are bound by the kidney in a few minutes; they refer to Sarre's study in which the left kidney, clamped during and ten minutes after injection, did *not* show the changes of nephrotoxic nephritis, although the right one did; (3) treatment with Strep. and tissues other than kidney "does not lead to significant renal lesions"; (4) renal lesions have been obtained by single injections of Strep-kidney mixtures, though not often and usually not of a severe nature; (5) there was "definite lack of parallelism between the dosage of antigen and the development of renal lesions that would be expected if the lesions were due to the toxic effects of the antigen. Furthermore, in animals, which had been treated previously with the antigen, immunity to the toxins could be expected to develop and therefore there would be less tendency for such lesions to be produced by reinfection. This was not found to be the case."

The Caveltis then proceeded to study the clinical and pathological manifestations of this nephrotoxic nephritis.[17] In the acute phase there were cylindruria, hematuria (most often microscopic),

proteinuria, and increased cell excretion, chiefly renal epithelial. These determinations were done with Addis counts, after normal standards were established in 500 rats, and in all cases in which there was nephrotoxic nephritis, the average count was many times normal. In the subacute and chronic phase the urinary findings were persistently abnormal, with increasing proteinuria and microscopic hematuria (sometimes intermittent); the sediments were in general quantitatively less than in the acute stage. There was also described a latent phase with or without abnormal urine sediments. In the acute phase there was often pronounced oliguria, at which times there was eye edema with "general puffiness." In the severe chronics, ascites and edema were often noted, with hypoproteinemia in some and lipemia in a few cases. Fatal or severely ill rats were in uremia; the anemia was usually marked. Clinically, therefore, this study shows a condition which both statically and throughout its course is identical with human glomerulonephritis.

Now let us look at their pathological findings. In the acute phase, the kidneys were hyperemic (very early) and then pale; they were often swollen and edematous and were usually increased in weight. Histologically, *all* the glomeruli were affected. They were somewhat enlarged with an increase in the number of endothelial and epithelial tuft cells. In many these cells were greatly swollen. The lumina contained desquamated epithelia, polymorphonuclear and monocytic white blood cells, and debris, and were narrowed and ischemic. Bowman's capsule showed epithelial swelling with some proliferation and adhesions; there were desquamated cells, erythrocytes and debris in the capsular space. The tubules showed minor degenerative changes and there was often some interstitial lymphocytic infiltration, especially around the small arteries.

In the subacute and chronic stage, "on the whole the changes were those of progressive obliteration of the glomeruli." The acute changes were present along with various degrees of hyalinization "more or less widespread." The glomeruli were regularly ischemic and there were occasional capsular crescents. The tubules often showed degenerative changes; there was diffuse lymphocytic infiltration of the interstitium. Of 208 rats, 127 had definite renal lesions, of which 85 were type 1 (acute glomerulonephritis). The remainder were the nonspecific type 2 changes, which have not been considered here.

These clinical and pathological findings have been described rather extensively because of the importance which this study has in regards the etiology of human glomerulonephritis. A comparison of these results with those findings in the human discussed earlier shows an exceedingly striking similarity in almost every detail, both in the cross-sectional and the longitudinal views.

Conclusions on the Etiology of Human Acute Glomerulonephritis. The facts on glomerulonephritis etiology as shown by the human evidence are as follows:

(1) A beta-hemolytic streptococcal infection almost invariably precedes acute glomerulonephritis.

(2) Usually this infection takes the form of an upper respiratory condition.

(3) In rare cases, other bacteria, such as the pneumococcus, Staph. aureus, or alpha Strep., may also precede glomerulonephritis.

(4) There is an interval of approximately two weeks between the onset of the Strep. infection and the onset of acute glomerulonephritis.

(5) In most of the cases the Strep. infection has disappeared well before the onset of glomerulonephritis.

(6) Bacteria have never been recovered from the kidneys of patients with acute glomerulonephritis, nor from the blood of such patients.

(7) "Subclinical" glomerulonephritis exists in many streptococcal postinfectious cases; this is shown by an abnormal urinary sediment.

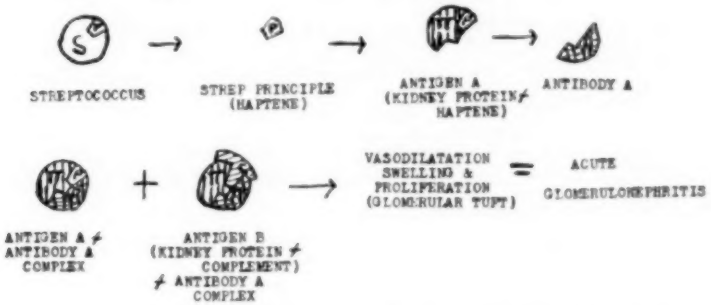
(8) Blood complement is reduced to subnormal levels in patients with acute glomerulonephritis and in no other condition, to our knowledge.

Remembering the experimental work presented above, we feel that the Strep. principle, liberated during the prodromal infection, in some way reacts with certain kidney protein(s), producing thereby an antigenic substance. This antigen acts as any foreign antigenic protein and incites antibody formation.

After one or two weeks, when this antibody titer reaches its peak (concomitant with the peak of other antistreptococcal antibodies), a "threshold" value is attained, and the antibody reacts with the kidney protein of the glomerular tuft, and then, possibly with the aid of blood complement, causes the sudden, diffuse reac-

tion to which we append the name of acute glomerulonephritis. We therefore are accepting as the animal counterpart of human acute glomerulonephritis, the strep-nephrotoxin nephritis of Cavelti and Schwentker, tying it to humans a bit more firmly with the work of Schwentker on human antibodies to rabbit kidneys.

One possible schematic illustration of the proposed reaction is as follows (this is obviously extremely theoretical, but the basic assumptions appear to us to be valid).


STREPTOCOCCUS
STREP PRINCIPLE (HAPTENE)
ANTIGEN A (KIDNEY PROTEIN ⚡ HAPTENE)
ANTIBODY A
ANTIGEN A ⚡ ANTIBODY A COMPLEX
ANTIGEN B (KIDNEY PROTEIN ⚡ COMPLEMENT) ⚡ ANTIBODY A COMPLEX
VASODILATATION SWELLING & PROLIFERATION (GLOMERULAR TUFT)
ACUTE GLOMERULONEPHRITIS

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CHLORAMPHENICOL IN WHOOPING COUGH. (Ugeskrift for Laeger, Copenhagen, 113: 776, June 14, 1951). From the results in 100 proved cases of whooping cough treated with chloramphenicol, Grandjean and Lassen conclude that this agent provides for the first time treatment for whooping cough effective in the great majority of cases. The treatment was followed by a sharp decrease in the attacks of coughing and by simultaneous notable improvement in the general condition. Chloramphenicol is regarded as indicated in all cases of whooping cough in infants and in graver cases in older children and adults. Determination of resistance of 45 whooping cough strains to chloramphenicol showed no resistant strain.—*Journal A.M.A.*

PEDIATRICS HALF A CENTURY AGO

From time to time the Archives, which was the first Children's Journal in the English language, will reprint contributions by the pioneers of the specialty over fifty years ago. It is believed that our readers will be interested in reviewing such early pediatric thought.

SOME POINTS IN INFANTILE TUBERCULOSIS*

The Frequency and Mode of Infection in Pulmonary Tuberculosis—A Study of the Cerebrospinal Fluid in Tuberculous Meningitis

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I. THE FREQUENCY AND MODE OF INFECTION IN PULMONARY TUBERCULOSIS

The frequency of pulmonary tuberculosis in infancy has not yet been fully appreciated because we have not been accustomed to look for it with sufficient thoroughness. More careful application of our means of diagnosis has made possible the recognition of tuberculosis in very many cases where otherwise it is likely to be overlooked, and has emphasized the fact that pulmonary tuberculosis is a very common disease in infants.

The means to which I refer particularly are the systematic search for the bacilli in the sputum in children who are known to have been exposed to infection, and the tuberculin test.

During the nineteen months ending May 1, 1907, 67 cases of pulmonary tuberculosis were treated in the Babies' Hospital; 62 of these being infants under two years, and 15 under six months of age.

The diagnosis rested upon finding the bacilli in the sputum in 54 of the cases; upon postmortem findings in 10; and of the remaining 3, one had tuberculous meningitis (bacilli found in the fluid drawn by lumbar puncture); one reacted to tuberculin, and the third gave typical clinical symptoms of pulmonary tuberculosis. In only one-half of these cases was there any consolidation in the lungs present at the time that the diagnosis was made, and

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in 9 cases there were no pulmonary signs whatever, the infants having been admitted for other conditions.

A demonstration of the tubercle bacillus in over 80 per cent of these cases when, according to the physical signs, the disease was not far advanced, brings up the question of the different means employed in obtaining the sputum in infants. This has been assumed to be, if not impossible, at least a difficult and uncertain procedure. Infants do not expectorate, but cough up the bronchial secretion into the pharynx and swallow it. Sputum must therefore be obtained from the pharynx or the esophagus; to seek for the bacilli in the vomitus, as has been recommended, is almost a hopeless task. For a time we tried passing a stomach tube and staining the esophageal mucus which adhered to the tube on withdrawal. This was satisfactory in some cases, but in many others it was not, as the mucus from the esophagus was apparently rubbed off as the tube was withdrawn through the mouth.

The method at present followed, and the one which has given the most satisfactory results, is to excite a cough by irritating the pharynx, and then to catch the sputum brought up into view, upon a bit of gauze or muslin. The cough may be excited by a spoon or a tongue depressor, or better, by a small bit of muslin in the jaws of an artery clamp. Upon this the secretion is easily secured when it is brought into view by the cough. Muslin is better than gauze or absorbent cotton. Swabs prepared as suggested are placed by the child's bedside and, when the nurse notices a severe paroxysm of coughing, the child is picked up and, if possible, the sputum is obtained. Inversion during the paroxysm of coughing sometimes causes the infant to discharge a considerable mass of mucus into a sputum cup. By the procedure mentioned it has not been found more difficult to obtain good sputum for examination than in corresponding stages of the disease in adults.

The source of infection in many of the hospital cases which form the basis of this paper, it was, of course, impossible to trace. It is, however, interesting to note that a definite history of tuberculosis in one or other parent existed in 21 cases, and that in 6 others there was positive evidence of the disease in some other member of the household; and in 2 others there was a somewhat doubtful history of tuberculosis. Direct contagion would therefore seem to be the explanation of a very large proportion of the cases,

it being shown in this series to have existed in at least 40 per cent of the children.

For the past year it has been the custom at the hospital to inquire carefully into the family history of all children admitted, and, if there was any evidence or even a strong suspicion of tuberculosis in either parent, a careful and repeated search was made for bacilli in the sputum of the infant admitted. In some of these children there was evidence of a slight amount of bronchitis; in others no evidence whatever of pulmonary disease.

The results of this routine examination have been rather surprising. If one or other parent was affected with tuberculosis, it has been very exceptional not to find tubercle bacilli in the sputum of the children; in a few of the cases where these were not found a positive reaction to tuberculin was obtained. This emphasizes the fact that the infant is exposed to house infection more intimately than any other member of the household. The older children are away at school, or out of doors at play; while the infant is very apt to be in charge of the invalid who is ill at home, and hence its opportunities for infection are greatly increased.

The relatively insignificant and infrequent intestinal lesions seen in the tuberculosis of children seem rather surprising when we consider for how long a period and in what numbers bacilli are coughed up and swallowed. It would appear that the intestinal tract is not very vulnerable to tuberculosis at this period of life.

The foregoing observations tend strongly to confirm one in the opinion that it is direct contagion which is responsible for most of the tuberculosis of infants rather than infection through milk or other foods.

II. A STUDY OF THE CEREBROSPINAL FLUID IN TUBERCULOUS MENINGITIS

The value of lumbar puncture as an aid to accurate diagnosis is now generally appreciated. It gives certainty in many irregular cases, where formerly tuberculous meningitis could only be suspected. Considerable difference of opinion has been at times expressed as to the frequency with which bacilli may be found in the fluid drawn by lumbar puncture. The results obtained by inoculating guinea-pigs with the fluid, indicated that the bacilli were nearly always present, but the general opinion has prevailed that

in a very large number of cases they could not be discovered by the microscope.

During the past fourteen months there have been treated in the Babies' Hospital 42 cases of tuberculous meningitis, in every one of which the tubercle bacilli have been found in the cerebrospinal fluid. This is, I think, a larger series of consecutive cases than has previously been reported. It may, therefore, be assumed that the bacilli are always present, and that they can be found provided a sufficient degree of care is exercised in searching for them.

Some important points in technique have been developed in the course of this study which are of some assistance in finding the bacilli. In withdrawing the fluid it has been customary to remove all that flows readily and receive it in several tubes, since the bacilli are much more likely to be found in the last portion drawn than in the first; probably because they are present in large number in the brain and come down with the fluid last removed. The number of bacilli is not usually great, and careful search is necessary, but not more than is required in hunting for the bacilli in the sputum. The average time consumed in this series was about one hour; in 2 cases a search of five or six hours was necessary; in only 3 of the entire number were the bacilli present in such numbers that practically every microscopical field revealed them.

The time of puncture is of some importance. The bacilli were usually more numerous in late puncture than in those made in the early stages of the disease, although they were sometimes found with the very earliest symptoms. In this series they were found by the first puncture in 34 cases; by the second puncture in 6 cases; and by the third puncture in 2 cases.

The technique of search followed at the Babies' Hospital is as follows: The fluid is allowed to stand in the test tube for twelve hours. If a film forms by the coagulation of fibrin in the fluid, this is fished out with a platinum loop and stained. Such film formation occurs in about half the cases, and in it the bacilli are pretty certain to be entangled. If no film forms, the sides of the tube are scraped with a platinum loop. If the bacilli are not found in this way, the fluid is centrifuged. The chances of success after centrifuging are greatly increased by adding to the fluid one or

two drops of blood. As a matter of routine, it has been found desirable to draw a single drop of blood with the very last fluid coming from the spinal canal. This is usually done by producing a slight movement with the needle before withdrawing it. The additional fibrin also aids the film formation and thus adds greatly to the facility of finding the bacilli.

Another procedure sometimes successful is to superimpose drops upon a slide. The first drop is placed and allowed to dry on; afterward a second one on the same spot, then a third, a fourth, and so on, and occasionally bacilli are found when their number is very small. Success depends largely upon the patience and cleverness of the observer.

The cells found in the cerebrospinal fluid in tuberculous meningitis are generally few in number, and these are usually mononuclear cells. Only twice in the 42 cases were cells present in sufficient numbers to give a marked turbidity to the fluid. This is in striking contrast to the fluid seen in cases of cerebrospinal meningitis and in those of pneumococcus meningitis.

It has been believed by many that the absence of glucose is of importance in diagnosticating meningitis from the normal cerebrospinal fluid. Fehling's test was applied in 32 cases. The presence of sugar was demonstrated in 15, but it was absent in 17 cases. No conclusions could, therefore, be drawn from the reaction.

It has been our custom to seek for bacilli in the sputum in every case of tuberculous meningitis, no matter whether pulmonary symptoms existed or not. They were found in 22 of the 42 cases, although in only 5 of these was there any consolidation of the lung, and in 9 there were no signs whatever in the chest. In the remainder there usually was some general bronchitis, which in most cases appeared late, and was more probably not of tuberculous origin.

DEPARTMENT OF ABSTRACTS

Ulin, A. W.; Nosal, J. L. and Martin, W. L.: Cholecystitis in Childhood. Report of a Case with Common Duct Calculi. (Journal American Medical Association, 147:1443, Dec. 8, 1951).

True cholecystitis and cholelithiasis are rare in children. However, in the differential diagnosis of jaundice and abdominal pain in children, the possibility of cholecystitis should be considered. Jaundice of hepatocellular origin is the more common and more important disease. Ill advised surgery for this condition might be fatal. The authors report the case of a 13-year-old white girl who complained of pain in the right upper quadrant for 24 hours. The pain had been present for one year. This pain was mild at first and periodic, occurring every 2 to 3 weeks. At first the pain did not radiate, later it became more severe, followed by nausea and vomiting and radiated around the right subcostal margin to the inferior angle of the right scapula. She also had several attacks of pain associated with jaundice and clay-colored stools. During one of these attacks a diagnosis of acute infectious hepatitis had been made. Examination revealed an acutely ill and dehydrated child. Tenderness and muscle guarding were noted in the right upper quadrant of the abdomen. A cholecystogram revealed non-opaque calculi in the gallbladder—a phrygian cap was present. A cholecystectomy and choledochostomy were done with excellent end results. Michael A. Brescia, M. D.

Hayman, C. R.; Rich, B. S. and Stark, E.: A Conservation of Hearing Program for School Children. (American Journal of Public Health, 41:1509, Dec. 1951).

Of 7,000 children that were tested by audiometry 1018 (14 per cent) showed some hearing loss. The majority had a mild loss of hearing, but 7.6 per cent had a severe or extreme loss of hearing. Chronic conduction deafness was found in 712 (72 per cent) patients, nearly all associated with upper respiratory infections. Partial obstruction of the eustachian tubes from infected tonsils and adenoids were present in 535; from infected adenoids alone in 132. Nerve deafness was found in 33 patients. Of 190 who had tonsil and adenoid operations, 69 per cent showed improve-

ment in hearing as compared to 33 per cent improvement in a similar group who did not have tonsil and adenoid operations. Hearing became worse in 2.6 per cent of those who had tonsil and adenoid operations, whereas it became worse in 20.9 per cent of those who had not had a tonsil and adenoid operation. 139 children received radium treatment of which group 54 per cent showed improvement in hearing.

MICHAEL A. BRESCIA, M.D.

ANDREWS, G. C.; DOMONKOS, A. N. AND POST, C.F.: TREATMENT OF ACNE VULGARIS. (Journal American Medical Association, 146:1107, July 21, 1951).

The authors feel that simple cases of oily seborrhea, comedones and papular acne (acne simplex) can be cured by a low fat diet, the administration of vitamin A and diethystilbestrol, the expression of comedones, and the use of orthodox local remedies such as lotio alba, sulfurated lime solution and remedies for the scalp. They also assume that in pustular, nodular and cystic cases the patients usually are sensitized to the Staphylococcus. They often harbor foci of infection which contribute to the pustulation and make it worse, if not being the sole cause. The authors further assume that the Staphylococci in pustular cases of acne differ greatly in their susceptibility to the various antibiotics. It has been brought out in the author's series of cases that cures of many severe nodular and cystic cases of acne can be accomplished by the use of sulfadiazine, sulfapyridine, aureomycin or terramycin without any other remedy This suggests, first, that we must revise some of the long held theories about acne, and, second, that infection by Staphylococci is the chief cause in some cases. Frequently occurring at an age when acne appears are focal infections in impacted and unerupted wisdom teeth and in tonsils. The chief features of the diet recommended are the avoidance of excessive amounts of fatty and fried foods and sweets and the eating of plenty of fruit, cereal, meat and vegetables. Chocolate, nuts, ice cream, cream, egg yolk and cheese should be avoided. Milk should be limited to a glass or two a day. Diet plays a negligible role in pustular and cystic cases. Where the patient is underweight, has poor posture, pallor and listlessness, injections of crude liver extract of vitamin B^{12} are given. Local treatment is of great importance. Supplementary cleansing of the skin with alcohol in

addition to the use of soap and water morning, noon and night will decrease the number of comedones and the amount of infection. MICHAEL A. BRESCIA, M.D.

NEUMANN, H. H.: MEDICAL PROGRESS AND DENTAL DECAY. (New York State Journal of Medicine, 51:1749, July 15, 1951).

In pediatric practice the physician is faced by the perennial question of how to prevent dental caries, before the services of the dentist are required. Observation of dental conditions universally in many ethnic groups indicates that this aim can be attained, although our knowledge is empiric and the explanations hypothetic: 1. The following factors are of no or doubtful significance in caries prevention: a nutritionally sound, well-balanced diet, the toothbrush and dental creams, sunshine and climatic conditions, and hereditary factors. 2. Passive preventive measures considered to influence caries incidence include fluorine applicable in various ways and carbohydrate reduction in the diet. 3. Active immunity or increased tooth resistance to caries may be achieved by vigorous mastication, not to be confused with prolonged mastication. Contrary to common belief, toast, biscuits, raw carrots and fruit and chewing gum as presently marketed are wholly inadequate to induce sustained and vigorous mastication. A soured, course black bread, with a heavy crust, regarded as fresh when a week old, or sugar cane are especially suitable, but both are hardly obtainable. The chewing of pencils, leather, or pieces of wood by children should be regarded as a wholesome instinct and not as a neurotic trait. AUTHOR'S SUMMARY.

HODSON, A. Z.: TERMINAL HEATING OF INFANT FORMULA. RETENTION OF NUTRITIVE VALUE OF MILK PROTEINS. (Journal American Dietetic Association, *27*:488, June 1951).

The nutritive value of the proteins of infant formulas before and after terminal heating have been compared by the rat-growth and rat-repletion methods. Data on formulas prepared from both evaporated milk and pasteurized milk were obtained. The data show that there was no measurable loss of protein nutritive value caused by terminal heating applied in accordance with stated methods.
AUTHORS' SUMMARY.

BANTON, A. H.: THE DEVELOPMENT OF MEDITERRANEAN ANEMIA. (Archives of Disease in Childhood, 26:235, June 1951).

The author reports on a detailed hematological study of two cases of Mediterranean anemia. These cases were studied shortly after birth and the development of the disease has been demonstrated in the early months of life. The author suggests that the anemia is a result of a defect in hemoglobin synthesis, due to the absence of some agent acting as a catalyst. The defect is variable in degree. From a genetic point of view, since the trait is inherited as a Mendelian dominant, this variable defect would be the link with the mutated gene causing the disease, and would be the fundamental error in Mediterranean anemia.

MICHAEL A. BRESCIA, M.D.

LYNCH, H. D. AND SNIVELY, W. D.: HYPOPROTEINOSIS OF CHILDHOOD. (Journal American Medical Association, 147:115, Sept. 8, 1951).

Hypoproteinosis in children is characterized by poor appetite, failure to gain weight and to grow normally, irritability, frequent gastro-intestinal upsets, including vomiting and constipation, repeated bouts of infectious diseases, dental caries and pallor. The dietary history, which is difficult to obtain adaquately, usually reveals liberal consumption of milk and carbohydrate foods, as well as adequate intake of minerals and vitamins, but insufficiency of solid protein foods, such as meat, eggs and cheese. Effective management not only requires a diet ample in protein but has educational and psychological facets as well.

MICHAEL A. BRESCIA, M.D.

COCHRAN, J. B.: THE ANEMIA OF RHEUMATIC FEVER. (British Medical Journal, 4732:637, Sept. 15, 1951).

The author studied 10 patients with acute rheumatic fever from a hematological standpoint. He found that the anemia which develops during the course of the acute illness is normocytic and normochromic or slightly hypochromic and is largely due to hydraemia without alteration in the total cell mass. The anemia is related to fluid shifts occurring during the rheumatic attack. The author suggests that the hydraemia and changes in the osmotic pressure of the plasma may be important factors in this and other anemias associated with infection. MICHAEL A. BRESCIA, M.D.

Captain Raymond Harvey Medal of Honor

THE 17TH INFANTRY REGIMENT was attacking Hill 1232 near Taemi-Doug, Korea. Able and Baker Companies became split by a Red-held ridge. Charlie Company, Captain Harvey commanding, was moving up to fill the gap when the dug-in Red guns pinned it down. Calling for covering fire,

Captain Harvey advanced *alone* through a hail of enemy bullets. One by one, he personally wiped out four emplacements of machine guns and automatic weapons. Then he caught a bullet through the lung. But he stayed on, refusing evacuation, until sure the objective had been won.

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"I hope you'll go on buying Bonds—many, many of them. For your Bonds—and our bayonets—are making America strong. And in today's cold-warring world, *peace is only for the strong.*"

★ ★ ★

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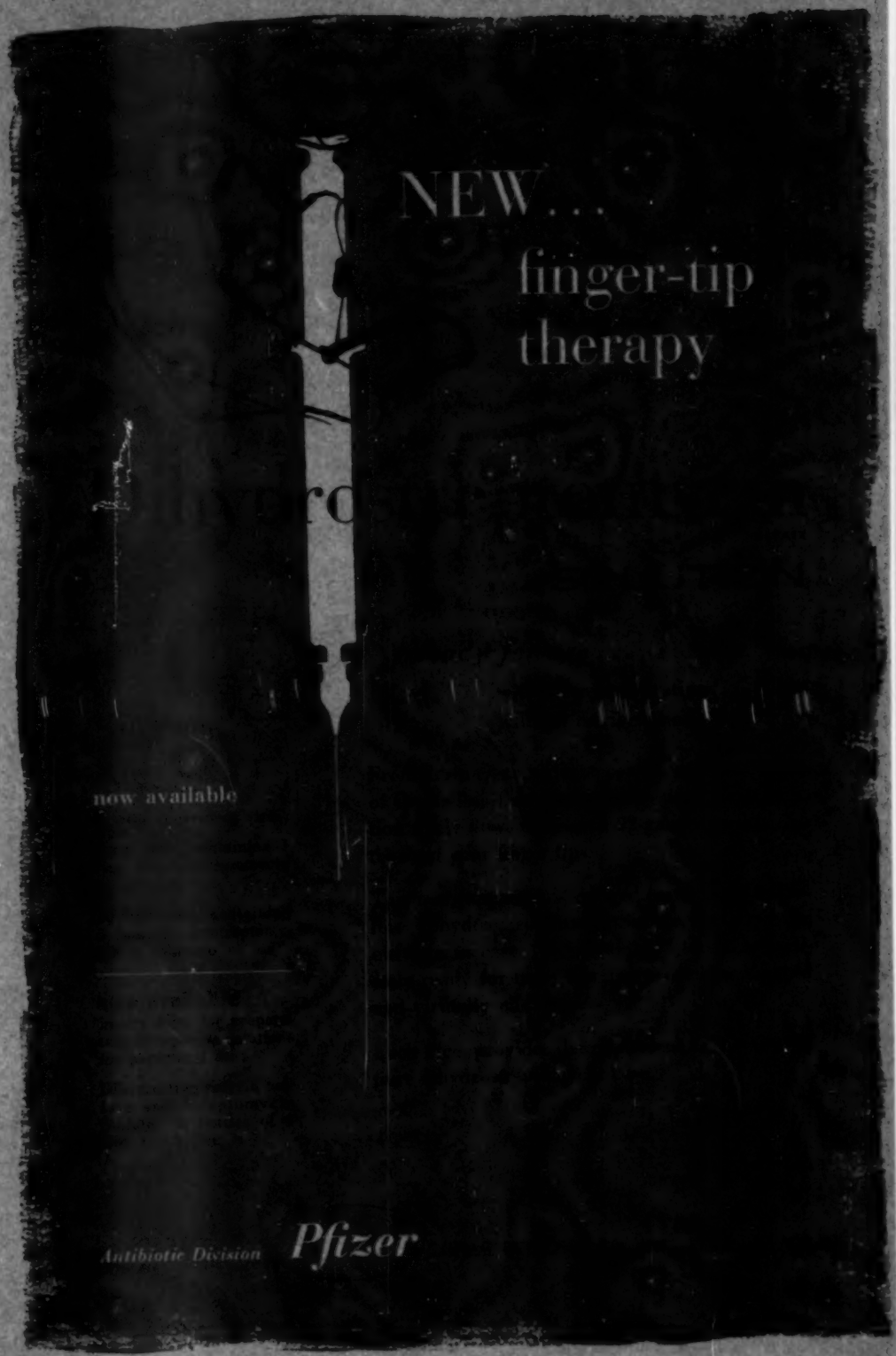
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